WHAT IS CLAIMED IS:

1. A receptor recognition factor implicated in the transcriptional stimulation of genes in target cells in response to the binding of a specific polypeptide ligand to its cellular receptor on said target cell, said receptor recognition factor having the following characteristics:

a) apparent direct interaction with the ligand-bound receptor and activation of one or more transcription factors capable of binding with a specific gene;

b) an activity demonstrably unaffected by the presence or concentration of second messengers;

c) direct interaction with tyrosine kinase domains; and

d) a perceived absence of interaction with G-proteins.

2. The receptor recognition factor of Claim 1 which is proteinaceous in composition.

3. The receptor recognition factor of Claim 1 which is cytoplasmic in origin.

4. The receptor recognition factor of Claim 1 which is a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:10 and SEQ ID NO:12.

5. The receptor recognition factor of Claim 1 which is derived from mammalian cells.

6. The receptor recognition factor of Claim 1 labeled with a detectable label.

7. The receptor recognition factor of Claim 6 wherein the label is selected from enzymes, chemicals which fluoresce and radioactive elements.

8. An antibody to a receptor recognition factor, the factor to which said antibody is raised having the following characteristics:

a) apparent direct interaction with the ligand-bound receptor and activation of one or more transcription factors capable of binding with a specific gene;

b) an activity demonstrably unaffected by the presence or concentration of second messengers; and

c) direct interaction with tyrosine kinase domains; and

d) a perceived absence of interaction with G-proteins.

9. The antibody of Claim 8 which is a polyclonal antibody.

10. The antibody of Claim 8 which is a monoclonal antibody.

11. An immortal cell line that produces a monoclonal antibody according to Claim 10.

12. The antibody of Claim 8 labeled with a detectable label.

13. The antibody of Claim 12 wherein the label is selected from enzymes, chemicals which fluoresce and radioactive elements.

14. A DNA sequence or degenerate variant thereof, which encodes a receptor recognition factor, or a fragment thereof, selected from the group consisting of:

(A) the DNA sequence of FIGURE 1;

(B) the DNA sequence of FIGURE 14;

(C) the DNA sequence of FIGURE 15;

(D) DNA sequences that hybridize to any of the foregoing DNA sequences under standard hybridization conditions; and

(E) DNA sequences that code on expression for an amino acid sequence encoded by any of the foregoing DNA sequences.

15. A recombinant DNA molecule comprising a DNA sequence or degenerate variant thereof, which encodes a receptor recognition factor, or a fragment thereof, selected from the group consisting of:

(A) the DNA sequence of FIGURE 1;

(B) the DNA sequence of FIGURE 14;

(C) the DNA sequence of FIGURE 15;

(D) DNA sequences that hybridize to any of the foregoing DNA sequences under standard hybridization conditions; and

(E) DNA sequences that code on expression for an amino acid sequence encoded by any of the foregoing DNA sequences.

16. The recombinant DNA molecule of either of Claims 14 or 15, wherein said DNA sequence is operatively linked to an expression control sequence.

17. The recombinant DNA molecule of Claim 16, wherein said expression control sequence is selected from the group consisting of the early or late promoters of SV40 or adenovirus, the lac system, the trp system, the TAC system, the TRC system, the major operator and promoter regions of phage λ, the control regions of fd coat protein, the promoter for 3-phosphoglycerate kinase, the promoters of acid phosphatase and the promoters of the yeast α-mating factors.

18. A probe capable of screening for the receptor recognition factor in alternate species prepared from the DNA sequence of Claim 14.

19. A unicellular host transformed with a recombinant DNA molecule comprising a DNA sequence or degenerate variant thereof, which encodes a receptor recognition factor, or a fragment thereof, selected from the group consisting of:

(A) the DNA sequence of FIGURE 1;

(B) the DNA sequence of FIGURE 14;

(C) the DNA sequence of FIGURE 15;

(D) DNA sequences that hybridize to any of the foregoing DNA sequences under standard hybridization conditions; and

(E) DNA sequences that code on expression for an amino acid sequence encoded by any of the foregoing DNA sequences;

wherein said DNA sequence is operatively linked to an expression control sequence.

20. The unicellular host of Claim 19 wherein the unicellular host is selected from the group consisting of E. coli, Pseudomonas, Bacillus, Streptomyces, yeasts, CHO, R1.1, B-W, L-M, COS 1, COS 7, BSC1, BSC40, and BMT10 cells, plant cells, insect cells, and human cells in tissue culture.

21. A method for detecting the presence or activity of a receptor recognition factor, said receptor recognition factor having the following characteristics: apparent direct interaction with the ligand-bound receptor and activation of one or more transcription factors capable of binding with a specific gene; an activity demonstrably unaffected by the presence or concentration of second messengers; direct interaction with tyrosine kinase domains; and a perceived absence of interaction with G-proteins, wherein said receptor recognition factor is measured by:

A. contacting a biological sample from a mammal in which the presence or activity of said receptor recognition factor is suspected with a binding partner of said receptor recognition factor under conditions that allow binding of said receptor recognition factor to said binding partner to occur; and

B. detecting whether binding has occurred between said receptor recognition factor from said sample and the binding partner;

wherein the detection of binding indicates that presence or activity of said receptor recognition factor in said sample.

22. A method for detecting the presence and activity of a polypeptide ligand associated with a given invasive stimulus in mammals comprising detecting the presence or activity of a receptor recognition factor according to the method of Claim 21, wherein detection of the presence or activity of the receptor recognition factor indicates the presence and activity of a polypeptide ligand associated with a given invasive stimulus in mammals.

23. The method of Claim 22 wherein said invasive stimulus is an infection.

24. The method of Claim 22 wherein said invasive stimulus is selected from the group consisting of viral infection, protozoan infection, tumorous mammalian cells, and toxins.

25. A method for detecting the binding sites for a receptor recognition factor, said receptor recognition factor having the following characteristics:

apparent direct interaction with the ligand-bound receptor and activation of one or more transcription factors capable of binding with a specific gene;

an activity demonstrably unaffected by the presence or concentration of second messengers;

direct interaction with tyrosine kinase domains; and

a perceived absence of interaction with G-proteins; wherein the binding sites for said receptor recognition factor are measured by:

A. placing a labeled receptor recognition factor sample in contact with a biological sample from a mammal in which binding sites for said receptor recognition factor are suspected;

B. examining said biological sample in binding studies for the presence of said labeled receptor recognition factor;

wherein the presence of said labeled recognition factor indicates a binding site for a receptor recognition factor.

26. A method of testing the ability of a drug or other entity to modulate the activity of a receptor recognition factor which comprises

A. culturing a colony of test cells which has a receptor for the receptor recognition factor in a growth medium containing the receptor recognition factor;

B. adding the drug under test; and

C. measuring the reactivity of said receptor recognition factor with the receptor on said colony of test cells,

wherein said receptor recognition factor has the following characteristics:

a) apparent direct interaction with the ligand-bound receptor and activation of one or more transcription factors capable of binding with a specific gene;

b) an activity demonstrably unaffected by the presence or concentration of second messengers;

c) direct interaction with tyrosine kinase domains; and

d) a perceived absence of interaction with G-proteins.

27. An assay system for screening drugs and other agents for ability to modulate the production of a receptor recognition factor, comprising:

A. culturing an observable cellular test colony inoculated with a drug or agent;

B. harvesting a supernatant from said cellular test colony; and

C. examining said supernatant for the presence of said receptor recognition factor wherein an increase or a decrease in a level of said receptor recognition factor indicates the ability of a drug to modulate the activity of said receptor recognition factor, said receptor recognition factor having the following characteristics:

a) apparent direct interaction with the ligand-bound receptor and activation of one or more transcription factors capable of binding with a specific gene;

b) an activity demonstrably unaffected by the presence or concentration of second messengers;

c) direct interaction with tyrosine kinase domains; and

d) a perceived absence of interaction with G-proteins.

28. A test kit for the demonstration of a receptor recognition factor in a eukaryotic cellular sample, comprising:

A. a predetermined amount of a detectably labelled specific binding partner of a receptor recognition factor, said receptor recognition factor having the following characteristics: apparent direct interaction with the ligand-bound receptor and activation of one or more transcription factors capable of binding with a specific gene; an activity demonstrably unaffected by the presence or concentration of second messengers; direct interaction with tyrosine kinase domains; and a perceived absence of interaction with G-proteins;

B. other reagents; and

C. directions for use of said kit.

29. A test kit for demonstrating the presence of a receptor recognition factor in a eukaryotic cellular sample, comprising:

A. a predetermined amount of a receptor recognition factor, said receptor recognition factor having the following characteristics: apparent direct interaction with the ligand-bound receptor and activation of one or more transcription factors capable of binding with a specific gene; an activity demonstrably unaffected by the presence or concentration of second messengers; direct interaction with tyrosine kinase domains; and a perceived absence of interaction with G-proteins;

B. a predetermined amount of a specific binding partner of said receptor recognition factor;

C. other reagents; and

D. directions for use of said kit;

wherein either said receptor recognition factor or said specific binding partner are detectably labelled.

30. The test kit of Claim 28 or 29 wherein said labeled immunochemically reactive component is selected from the group consisting of polyclonal antibodies to the receptor recognition factor, monoclonal antibodies to the receptor recognition factor, fragments thereof, and mixtures thereof.

31. A method of preventing and/or treating cellular debilitations, derangements and/or dysfunctions and/or other disease states in mammals, comprising administering to a mammal a therapeutically effective amount of a material selected from the group consisting of a receptor recognition factor, an agent capable of promoting the production and/or activity of said receptor recognition factor, an agent capable of mimicking the activity of said receptor recognition factor, an agent capable of inhibiting the production of said receptor recognition factor, and mixtures thereof, or a specific binding partner thereto, said receptor recognition factor having the following characteristics:

a) apparent direct interaction with the ligand-bound receptor and activation of one or more transcription factors capable of binding with a specific gene;

b) an activity demonstrably unaffected by the presence or concentration of second messengers;

c) direct interaction with tyrosine kinase domains; and

d) a perceived absence of interaction with G-proteins.

32. The method of Claim 31 wherein said disease states include chronic viral hepatitis, hairy cell leukemia, and tumorous conditions.

33. The method of Claim 31 wherein said receptor recognition factor is administered to modulate the course of therapy where interferon is being administered as the primary therapeutic agent.

34. The method of Claim 31 wherein said receptor recognition factor is administered to modulate the course of therapy where interferon is being co-administered with one or more additional therapeutic agents.

35. A pharmaceutical composition for the treatment of cellular debilitation, derangement and/or dysfunction in mammals, comprising:

A. a therapeutically effective amount of a material selected from the group consisting of a receptor recognition factor, an agent capable of promoting the production and/or activity of said receptor recognition factor, an agent capable of mimicking the activity of said receptor recognition factor, an agent capable of inhibiting the production of said receptor recognition factor, and mixtures thereof, or a specific binding partner thereto, said receptor recognition factor having the following characteristics: apparent direct interaction with the ligand-bound receptor and activation of one or more transcription factors capable of binding with a specific gene; an activity demonstrably unaffected by the presence or concentration of second messengers; direct interaction with tyrosine kinase domains; and a perceived absence of interaction with G-proteins; and

B. a pharmaceutically acceptable carrier.

36. A receptor recognition factor implicated in the transcriptional stimulation of genes in target cells in response to the binding of a specific polypeptide ligand to its cellular receptor on said target cell, said receptor recognition factor having the following properties:

a) it is present in cytoplasm;

b) it undergoes tyrosine phosphorylation upon treatment of cells with IFNα;

c) it activates transcription of an interferon stimulated gene;

d) it stimulates either an ISRE-dependent or a gamma activated site (GAS)-dependent transcription in vivo;

e) it interacts with IFNα cellular receptors, and

f) it undergoes nuclear translocation upon stimulation of the IFN cellular receptors with IFNα.

37. A receptor recognition factor implicated in the transcriptional stimulation of genes in target cells in response to the binding of an interferon or interferon-related polypeptide ligand to its cellular receptor on said target cell, said receptor recognition factor having the following properties:

a) it is present in vivo in mammalian cytoplasm before activation of cellular IFN receptors;

b) it contains tyrosine sites that are phosphorylated in response to IFN stimulation of IFN receptors;

c) it has a molecular weight selected from the group consisting of 48kD, 84kD, 91kD and 113kD, or an amino acid sequence selected from the group consisting of SEQ ID NO:10 and SEQ ID NO:12, and

d) when phosphorylated, it recognizes an ISRE in the cell nucleus.

38. The receptor recognition factor of either of Claims 36 or 37 in phosphorylated form.

39. An antibody which recognizes a phosphorylated ISGF3 polypeptide or a fragment thereof in phosphorylated form.

40. An antibody produced by injecting a substantially immunocompetent host with an antibody-producing effective amount of an ISGF3 polypeptide, and harvesting said antibody, said ISGF3 polypeptide having the following properties:

a) it has a molecular weight of about 48kD, 84Kd, 91 Kd or 113kD or an amino acid sequence selected from the group consisting of SEQ ID NO:10 and SEQ ID NO:12;

b) it can be isolated from mammalian cytoplasm;

c) it contains tyrosine residues that are subject to phosphorylation in vivo upon treatment of cells with IFNα;

d) it can activate transcription of an interferon stimulated gene in vivo;

e) it can stimulate ISRE-dependent transcription in vivo;

f) it can interact with IFNα cellular receptors, and

g) it can undergo nuclear translocation upon stimulation of IFN cellular receptors with IFNα.

41. The antibody of either of Claims 39 or 40 which is monoclonal.

42. The antibody of either of Claims 39 or 40 which is polyclonal.

43. A recombinant virus transformed with the DNA molecule, or a derivative or fragment thereof, in accordance with Claim 14.

44. A recombinant virus transformed with the DNA molecule, or a derivative or fragment thereof, in accordance with Claim 15.

45. A method of enhancing IFNα activity in a mammal in need of such treatment, comprising administering to said mammal an effective amount of a compound which (a) enhances the phosphorylation of intracellular ISGF3 proteins to form ISGF3-protein phosphates, or (b) inhibits the activity of a phosphatase enzyme which would otherwise reduce the level of phosphorylated ISGF3 proteins.

46. A method of treating (a) chronic viral hepatitis or (b) hairy cell leukemia, in a mammal in need of such treatment, comprising administering to said mammal an effective amount of a compound which (a) enhances the phosphorylation of ISGF3 proteins, or (b) decreases the level of phosphate removal from phosphorylated ISGF3 proteins.

47. The method of Claim 45 wherein the activity of exogenous IFNα is enhanced.

48. The method of Claim 45 wherein the activity of endogenous IFNα is enhanced.

49. The method of Claim 47 wherein the compound and IFNα are administered concurrently to the mammal in need of such treatment.

50. A method of determining the interferon-related pharmacological activity of a compound comprising:

administering the compound to a mammal;

determining the level of phosphorylated ISGF3 proteins present; and

comparing the level of ISGF3 protein-phosphate to a standard.

51. In a method of treating hepatitis or leukemia in a mammal, wherein IFNα is administered in an amount effective for treating such hepatitis or leukemia, the improvement comprising administering to said mammal an ISGF3 protein or a derivative thereof in an amount effective for enhancing the activity of said IFNα.

52. The method of Claim 51 wherein a derivative of said ISGF3 protein is administered.

53. The method of Claim 51 wherein an ISGF3 protein is administered, having a molecular weight of about 48 kD, 84kD, 91kD or 113kD.

54. The method of Claim 52 wherein the derivative is a phosphorylated ISGF3 protein.

55. The recombinant DNA molecule of Claim 16 comprising plasmid pGEX-3X, clone E3 or plasmid pGEX-3X, clone E4.

56. An antisense nucleic acid against a receptor recognition factor mRNA comprising a nucleic acid sequence hybridizing to said mRNA.

1 '57. The antisense nucleic acid of Claim 56 which is RNA.

1 58. The antisense nucleic acid of Claim 56 which is DNA.

1 59. The antisense nucleic acid of Claim 56 which binds to the initiation codon
2 of any of said mRNAs.

1 60. A recombinant DNA molecule having a DNA sequence which, on
2 transcription, produces an antisense ribonucleic acid against a receptor recognition
3 factor mRNA, said antisense ribonucleic acid comprising an nucleic acid sequence
4 capable of hybridizing to said mRNA.

1 61. A receptor recognition factor-producing cell line transfected with the
2 recombinant DNA molecule of Claim 60.

1 62. A method for creating a cell line which exhibits reduced expression of a
2 receptor recognition factor, comprising transfecting a recognition factor-producing
3 cell line with a recombinant DNA molecule of claim 60.

1 63. A ribozyme that cleaves receptor recognition factor mRNA.

1 64. The ribozyme of Claim 63 which is a Tetrahymena-type ribozyme.

1 65. The ribozyme of Claim 63 which is a Hammerhead-type ribozyme.

1 66. A recombinant DNA molecule having a DNA sequence which, upon
2 transcription, produces the ribozyme of claim 63.

1 67. A receptor recognition factor-producing cell line transfected with the
2 recombinant DNA molecule of claim 66.

68. A method for creating a cell line which exhibits reduced expression of a receptor recognition factor, comprising transfecting a recognition factor-producing cell line with the recombinant DNA molecule of claim 63.

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